REMARKS

Status of the claims

Claims 10-11, 13-14 and 42-43 are pending and are rejected herein. Claims 1-9, 11-12 15-41 and 43 are are canceled. Claims 10, 13-14, 42, and 44 are amended. No new matter was added in any claim amendment.

Amendments to the claims

Claims 10, 14 and 44 were amended to limit the sequence to SEQ ID NO: 4. Claims 13 and 42 were amended to limit the peptide(s) to those encoded by DNA fragment or DNA, respectively, with the sequence shown in SEQ ID NO: 2. Claims 1-9, 11-12, 15-41, and 43 are canceled.

Amendments to the specification

Applicants have amended the specification to remove reference to a URL. Applicants also have amended the specification and the sequence listing to correct errors in identification of sequences shown in SEQ ID NOS: 1-4. Parts of the specification, e.g., the Summary and the Detailed Description and Sequence Listing incorrectly identify SEQ ID NOS: 1, 3 as being part of the complementary determining region-3 (CDR3) in the Vβ family (BV14 gene) and SEQ ID NOS: 2 and 4 as being part of the complementary determining region-3 (CDR3) in the Vβ family (BV14 gene).

However, the data presented in Example 11 and in Tables 4 and 5 clearly demonstrates that the DNA of SEQ ID NO: 1 and peptide of SEQ ID NO: 3

belong to BV-16 (see PP 0087 and bold portion of SEQ ID NO: 93 in Table 4) and that the DNA of SEQ ID NO: 2 and peptide of SEQ ID NO: 4 belong to BV14 (see PP 0087 and bold portion of SEQ ID NO: 129 in Table 5). Applicants have amended the specification and corrected the description in field <223> of SEQ ID NOS: 1-4 in the sequence listing. Applicants enclose the replacement Sequence Listing, a Sequence Compliance Statement as well as a computer readable form (CRF) of the Sequence Listing. No new matter was added in these amendments.

Objection to the specification

The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. Applicants have amended the specification to remove the hyperlink, as discussed supra. Accordingly, in view of the amendment to the specification, Applicants respectfully request that the objection to the specification be withdrawn.

The 35 U.S.C. §112, first paragraph rejection

Claims 13 and 42-43 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description. Claims 13 and 42-44 are rejected under 35 U.S.C. §112, first paragraph, because the specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. Applicants traverse this rejection.

The Examiner states that there is insufficient written description to demonstrate that Applicants were in possession of a genus of peptides "derived from a CDR3 region or from a single chain T cell receptor variable region or

fragments therefrom. The Examiner also states that given the breadth of the claims drawn to vaccines or pharmaceutical compositions comprising any peptide derived from a CDR3 of a BV14 or BV16 TCR from an individual suffering from rheumatoid arthritis, the unpredictability in the art in using any CDR3 sequence for vaccination and the lack of working examples, undue experimentation would be required to practice the invention.

Applicants have canceled claim 43. Claims 13 and 42 are amended to recite that the peptide(s) is encoded by a DNA with the sequence shown in SEQ ID NO: 2. The specification, as amended and discussed supra, discloses SEQ ID NO: 2 and that it encodes the peptide with SEQ ID NO: 4 and therefore meets the written description requirement. Furthermore, the instant specification demonstrates that the peptide with SEQ ID NO: 4 is a sequence characteristic of T cells associated wth rheumatoid arthritis. Individuals with rheumatoid arthritis expressing the CDR3 of T cell receptor beta-chain BV14 gene comprising DNA fragment SEQ ID NO:.2, which encodes the T cell receptor sequence of SEQ ID NO: 4, do so at a substantially higher level than in control or normal individuals. Therefore, the peptide of SEQ ID NO: 4 would be useful in a therapeutic strategy against rheumatoid arthritis, such as administering the peptide as a vaccine or pharmaceutical composition in an amount effective to elicit an immune response against cells expressing a CDR3 protein comprising the peptide of SEQ ID NO: 4. As such, a person having ordinary skill in this art could easily make and determine the efficacy of the vaccines or pharmaceutical compositions encompassed by the claims using standard and well known assays without undue experimentation. Accordingly, in view of the claim amendment and arguments presented herein,

Applicants respectfully request that the rejection of claims 13 and 42 under 35 U.S.C. §112, first paragraph, be withdrawn.

The 35 U.S.C. §102(a) rejection

Claims 10-11 and 13-14 are rejected under 35 U.S.C. §102(a) as being anticipated by GenPept Accession No. **CAD67333**, Feb. 2003, as evidence by Oxford University Press, "peptide" definition. Applicants respectfully traverse this rejection.

The Examiner states that the **CAD67333** reference teaches an amino acid sequence having the amino acid sequence of SEQ ID No; 4 of the instant application at residues 92-98. The Examiner also states that the Oxford dictionary defines a peptide as any compound with two or more amino acids linked together, the sequence taught by **CAD6733** is a peptide. The Examiner further states that **CAD67333** teaches a peptide identical in structure to the instantly claimed peptide.

CAD67333 teaches a 253 amino acid putative integral membrane protein from *Tropheryma whipplei*. Applicants have canceled claims 11 and 43. Amended claim 10 is drawn to a substantially pure and isolated peptide with the sequence of SEQ ID NO: 4. Amended claim 13 is drawn to a vaccine comprising at least one peptide encoded by DNA with the sequence of SEQ ID NO: 2, as discussed supra. Amended claim 14 is drawn to a peptide with the amino acid sequence of SEQ ID NO: 4.

It is well established that to anticipate a claim, each and every claim element must be taught expressly or inherently in a single reference. The

disclosure in **CAD67333** specifically defines the disclosed sequence as a protein which contains at positions 92-98 the amino acids of the instant SEQ ID NO: 4. Respectfully, the Examiner is using the Oxford dictionary to refute the specifically stated definition of the amino acid sequence of **CAD6733** as a protein. Applicants respectfully submit that the use of multiple references in a §102(a) rejection is to explain but not expand the meaning of terms and phrases used in the reference relied upon as anticipatory of the claims (MPEP 2131.01 (II)).

Therefore, Applicants state that, as defined in the reference, **CAD6733** is a protein and that any fragment of the protein would be a peptide thereof. **CAD67333** does not teach a substantially pure and isolated peptide with the sequence shown in SEQ ID NO: 4. In addition, **CAD67333** does not teach nor suggest a DNA or nucleic acid sequence with the sequence of SEQ ID NO: 2, as recited in amended claim 13.

Thus, **CAD67333** (or the Oxford dictionary definition of peptide) does not teach all the claim elements of amended claims 10 and 13-14. Therefore, **CAD67333** is not prior art under 35 U.S.C. §102(a). Accordingly, in view of the claim amendment and arguments presented herein, Applicants respectfully request that the rejection of claims 10 and 13-14 under 35 U.S.C. §102(a) be withdrawn.

The 35 U.S.C. §103(a) rejection

Claims 42-44 are rejected under 35 U.S.C. §103(a) as being unpatentable over **CAD67333**, Feb. 2003, in view of **Cleland** et al. (Critical

Reviews in Therapeutic Drug Carrier Systems (1993), Vol. 10: 307-377). Applicants respectfully traverse this rejection.

The Examiner states that **CAD67333** teaches the peptide sequence of SEQ ID NO: 4, but does not teach a composition comprising a pharmaceutically acceptable carrier. The Examiner states that **Cleland** et al. teach that protein formulations containing buffer components and excipients prevent the formation of aggregates that can cause an altered half-life (pg. 317) and that excipients can be used in pharmaceutical formulations (pgs. 317, 319). Therefore, the Examiner maintains it would be prima facie obvious to one of ordinary skill in the art to make a formulation comprising the protein taught by **CAD67333** and a pharmaceutically acceptable excipients taught by **Cleland** et al. to prevent the formation of aggregates that can cause altered half-life of a protein formulation. Applicants respectfully disagree.

CAD67333 is described by Applicants supra. **Cleland** et al. teach methods to develop stable protein formulations, including pharmaceutical formulations, using buffering components and excipients (pg. 317). Applicants have canceled claim 43. Amended claim 42 is drawn to a pharmaceutical composition comprising an immunologically effective amount of a peptide encoded by a DNA with the sequence shown in SEQ ID NO: 2 and a pharmaceutically acceptable carrier.

To establish a prima facie case of obviousness, the combination of references must fairly teach all the claim elements, there must be a suggestion or motivation in the combination of references or general knowledge to modify or combine reference teachings and there must be a reasonable expectation of

succes in making the combination not found in the Applicants' disclosure. As discussed supra, **CAD67333** neither teaches nor suggests the DNA of SEQ ID NO: 2. Combining **CAD67333** with **Cleland** et al. does not remedy this deficiency. Furthermore, the protein disclosed in **CAD67333** is from *Tropheryma whipplei* which causes Whipple's disease and is not associated with rheumatoid arthritis.

At a minimum, one of ordinary skill in the art would not be motivated to view this protein as a source of peptides formulated as pharmaceutical compositions useful against rheumatoid arthritis without Applicants' disclosure that DNA of SEQ ID NO: 2 encodes a peptide of SEQ ID NO: 4 characteristic of T cells associated with rheumatoid arthritis. Although the sequence of SEQ ID NO: 4 is found in **CAD67333** at amino acids 92-98, one of ordinary skill in the art would have no basis to select this **CAD67333** fragment. At best, the combination of **CAD67333** and **Cleland** et al. references might motivate one of ordinary skill in the art to formulate the whole protein of **CAD6733** with an excipient to increase its stability.

Clearly, the combination of **CAD67333** and **Cleland** et al. does not teach nor suggest DNA with SEQ ID NO: 4. Thus, a prima facie case of obviousness has not been established. In addition, amended claim 44 depends directly from amended independent claim 42 and limits the encoded peptide to the sequence of SEQ ID NO: 4. If the combination of **CAD6733** and **Cleland** et al. cannot render amended independent claim 42 obvious, then neither is dependent amended claim 44 rendered obvious by the combination. Accordingly, in view of the claim amendment and arguments presented herein, Applicants

respectfully request that the rejection of claims 42 and 44 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed May 24, 2006. Applicants enclose a paper copy of the corrected Sequence Listing, a Compliance Statement and a CRF of the Sequence Listing. Applicants submit that claims 10, 13-14, 42, and 44, as presented herein, are in condition for allowance. Accordingly, Applicants request that claims 10, 13-14, 42, and 44 be passed to issuance. Should any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution. Please charge the $750 revival fee for the Petition to Revive an Unintentionally Abandoned Application to the credit card identified on the enclosed Form PTO-2038. **Only in the absence** of Form PTO-2038, please debit any applicable fees from Deposit Account No. 07-1185 upon which the undersigned attorney is allowed to draw.

Respectfully submitted,

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